## Thirdhand Smoke Exposure and Health Effects

Lara Gundel, Hugo Destaillats, Mohamad Sleiman, Jennifer Logue and Brett Singer

Indoor Environment Group
Energy Analysis & Environmental Impacts Division
Energy Technologies Area





## THS is receiving increasing attention ...





ou may never have heard of thirdhand a flurry of coverage in the international media<sup>2,3</sup>. New York Times, "the invisible yet toxic brew of which plaintiffs are citing these alleged dangers, <sup>8,0</sup> gases and particles clineing to smokers' hair and despite a lack of human health studies on the lone dothing, not to mention cushions and carpet- term health effects of THS exposure. ing, that lingers long after secondhand smoke So how dangerous might THS really be? The [SHS] has cleared from a room.\*1 Recent research answer, still to be pronounced, will depend on exploring potential dangers of THS has received many factor

smelled it. THS is, in the words of The States, court cases are beginning to appear in

in dust after tobacco has been smoked, 2) are re-emitted back into the gas phase, or 3) reac

#### **AFTER THE** SMOKE CLEARS

**INDOOR CHEMISTRY: Tobacco** residues react with chemicals in air to form dangerous products

ONSMOKERS may have a new worrythirdhand smoke. Nicotine residues on indoor surfaces can react with nitrous acid in the air to form carcinogenic nitrosamines not present in fresh tobacco smoke, chemists at Lawrence Berkeley National Laboratory have demonstrated.

"The residual smoke on surfaces appears to become even more toxic through reactions with other atmospheric chemicals," says K. Michael Cummings,

Reaction of surfacebound nicotine with nitrous acid can form one of three tobacco-specific nitrosamines. The nitrosamino aldehyde shown is the primary product.

a secondhand-smoke expert at Roswell Park Cancer Institute in Buffalo. "The assumption was with time the material would become less, not more, harmful,"

More than 30 years ago, Stephen S. Hecht and coworkers of the University of Minnesota first showed that nicotine reacts with nitrous acid in aqueous solution. A new study shows that such reactions can also happen with nicotine left behind from tobacco smoke and nitrous acid in the air. "We are describing a system in which these reactions can take place on indoor surfaces," says Hugo Destaillats, a chemist at LBNL (Proc. Natl. Acad. Sci. USA, DOI: 10.1073/pnas.0912820107).

Destaillats, Lara A. Gundel, Mohamed Sleiman, and coworkers measured nitrosamines formed by the reaction of nicotine adsorbed on surfaces with nitrous acid in the air. They took samples from a nicotine-coated model cellulose surface and from surfaces in the cab of a smoker's truck. Three tobacco-specific nitrosamines were the main products of the reaction.

The researchers propose the following mechanism for the reaction: NO\* removes an electron from the pyrrolidine nitrogen of nicotine to form an unstable cation. Then, a second NO\* abstracts H from one of the three \alpha-carbons to form an iminium ion. Subsequent reactions with adsorbed water and nitrous acid vapors yield the nitrosamines.

In addition, they found secondary products resulting from decomposition of the nitrosamines. One of these compounds, a stable pyrazole formed from the decomposition of one of the nitrosamines that has not

> been observed in fresh tobacco smoke, could serve as a tracer for thirdhand smoke, the authors

"Since nicotine readily adsorbs to surfaces and nitrogen oxides are ubiquitous, their findings may have some relevance to contami-

nation by thirdhand smoke," Hecht says, "Research would be necessary to demonstrate whether, for example, infants in homes that permitted smoking were receiving significant exposures by this route. I personally feel that exposure by this route would be minimal, but the studies need to be carried out."

Destaillats emphasizes that this study addresses only the chemistry. "Our study should incite some of our colleagues to determine whether exposure to these reactive residues and by-products of these reactive residues can be harmful," he says, -CELIA ARNAUD

Review



#### Thirdhand Tobacco Smoke: Emerging Evidence and Arguments for a Multidisciplinary Research Agenda

Georg E. Matt, Penelope J. E. Quintana, Hugo Destaillats, Lara A. Gundel, Mohamad Sleiman, Brett C. Singer, Peyton Jacob III, Neal Benowitz, Jonathan P. Winickoff, Virender Rehan, Prue Talbot, Suzaynn Schick, Jonathan Samet, Yinsheng Wang, Bo Hang, Manuela Martins-Green, 11 James F. Pankow, 12 and Melbourne F. Hovell<sup>2</sup>

## ... and impacting the media, regulators and advocacy groups

## Bill bans smoking at all times in home day cares

By FENIT NIRAPPIL - Associated Press - Monday, April 21, 2014

The Washington Post

SACRAMENTO, Calif. (AP) - The Assembly approved a bill Monday that would ban smoking inside home day care centers even after the children have left, a regulation that targets lingering "third-hand smoke" and has been adopted by 12 other states.





## The California Consortium on THS



#### **Principal Investigator**

N. Benowitz (UCSF)

L. Gundel (LBNL)



#### Chemistry, Remediation DNA damage

- H. Destaillats
  - L. Gundel,
- M. Sleiman,
- J. Logue,
- J. Pankow (PSU)

  <u>B. Hang</u>

University of California San Francisco

## Human exposure Biomarkers

N. Benowitz
P. Jacob III
S. Schick



#### Toxicology Health effects

P. Talbot
M. Martins-Green
N. zur Nieden
(affiliated)



#### Exposure Behavior Persistence

G.Matt M. Hovell P. Quintana E. Hoh



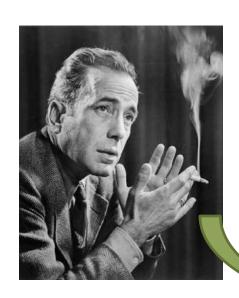
## Exposure Policy Economics

J. Samet H. Wipfli

## What is thirdhand smoke (THS)?

## Working definition:

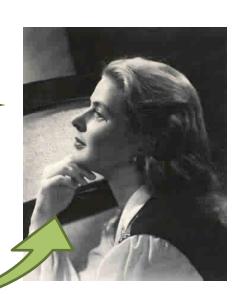
## Tobacco toxins that <u>remain</u>, <u>react</u>, <u>re-emit</u> and/or <u>re-suspend</u> in indoor environments



### Secondhand smoke

- ✓ primarily inhalation
- ✓ short time scales (min to hs)





## Thirdhand exposures

- ✓ inhalation + dermal + ingestion
- ✓ long time scales: up to months

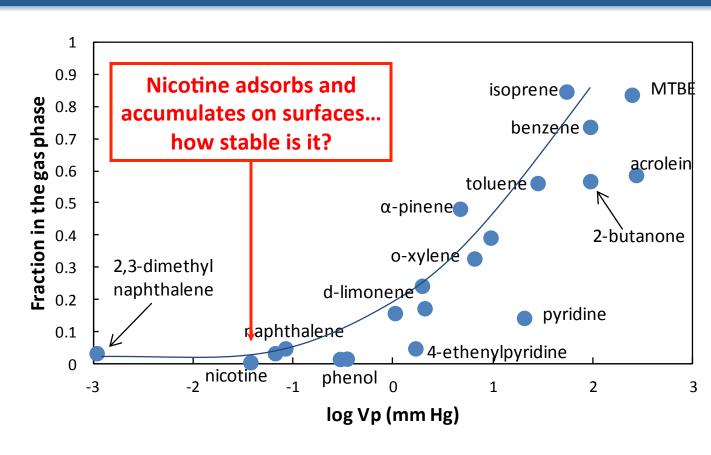
## Our goals

- 1. Refine the definition of THS
- 2. Understand THS chemistry on indoor surfaces (e.g., nicotine reaction with  $O_3$  and other species)
- 3. Identify key inhalable THS constituents (harmful pollutants and THS tracers)
- 4. Quantify the harm caused by secondhand and thirdhand smoke
- 5. Evaluate THS remediation approaches

## Berkeley Lab's early work on THS

Partitioning of tobacco pollutants in furnished 50-m<sup>3</sup> chamber

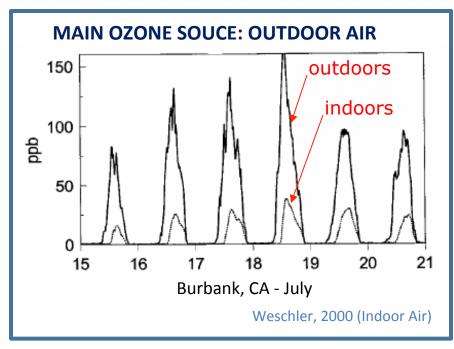




"...airborne concentration of some ETS constituents can be significantly affected by sorptive interactions with indoor surfaces... Exposure-relevant emission factors implicitly incorporate sorption effects under realistic furnishing and ventilation conditions."

Singer et al, ES&T 2002 Singer et al, Atmos Environ 2003 Singer et al, Atmos Environ 2004 Nazaroff and Singer, JEAEE 2004 Singer et al, Atmos Environ 2007

### What is the effect of indoor ozone?





## 1) Ozone quickly oxidizes nicotine on indoor surfaces



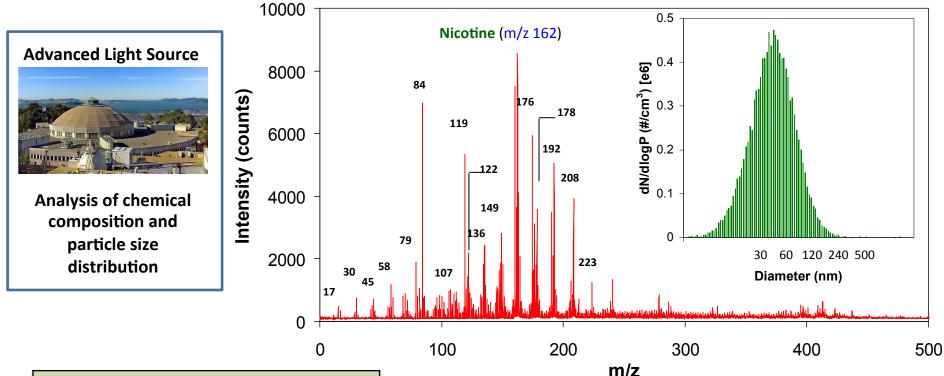




2) We observed gas phase and particle-bound byproducts: cotinine, nicotinaldehyde, N-methyl formamide

Destaillats et al. ES&T 2006

## Ozone reactions with nicotine create new ultrafine particles

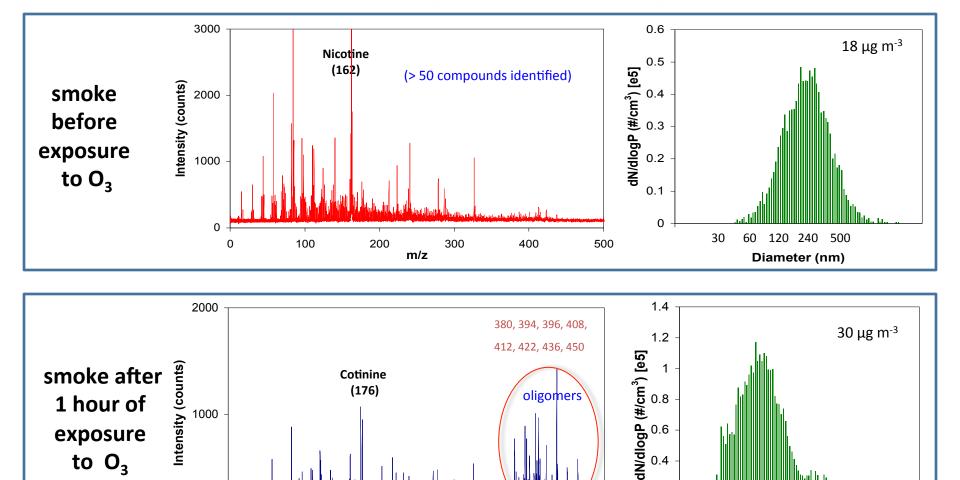


[O <sub>3</sub> ] <sub>0</sub> = 100 ppb	Humidified air (RH: 50%)
Secondary Organic Aerosol (SOA) yield (%)	9.2
Concentration (µg m <sup>-3</sup> )	186
Diameter (nm)	70 and 120

... also oxidation products that are more irritating than nicotine.

Sleiman et al., Atmos. Environ. 2010

## Ozone reactions with full cigarette smoke: smaller particles & more complex compounds



0.2

500

120 240

Diameter (nm)

500

60

100

200

300

m/z

400

(< 100 ppbv)

# Carcinogens are created by reaction of nicotine with nitrous acid (HONO) from cooking with gas

#### Sources of HONO and NOx

- ☐ combustion (indoor and outdoor)
- ☐ heterogeneous conversion of NOx on indoor surfaces yielding HONO (g)
- ☐ typical indoor HONO levels are 10-40 ppb (higher than outdoors)



#### Formation of nitrosamines

☐ Reaction of surface-bound nicotine with HONO formed carcinogenic tobacco-specific nitrosamines (TSNAs)

$$\begin{array}{c|c}
NNK & NNA \\
O & CH_3
\end{array}$$

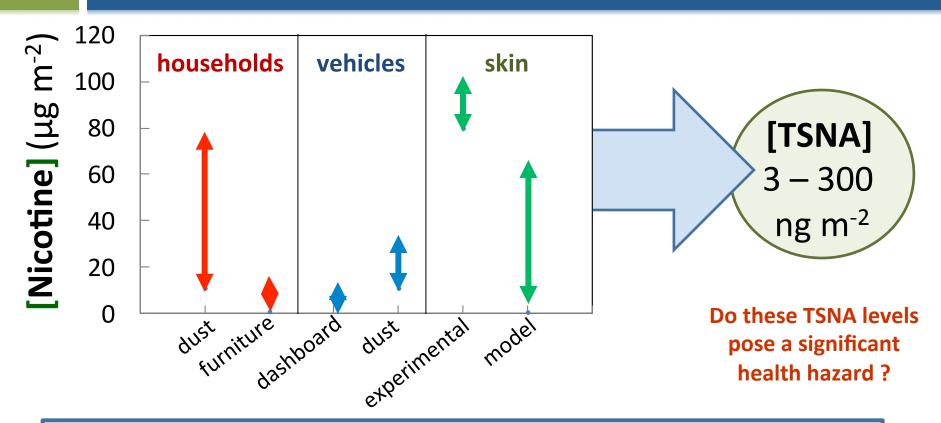
$$\begin{array}{c|c}
N & C \leq O \\
N & N = O
\end{array}$$

$$\begin{array}{c|c}
C \neq O \\
N & N = O
\end{array}$$

- ☐ NNA is not present in fresh smoke
- ☐ TSNAs were found on cabin surfaces of a smoker's vehicle
- ☐ We determined the TSNA yield of formation

Sleiman et al., PNAS, 2010

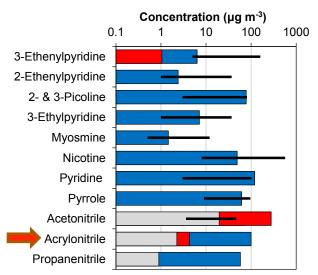
## Implications for indoor exposures



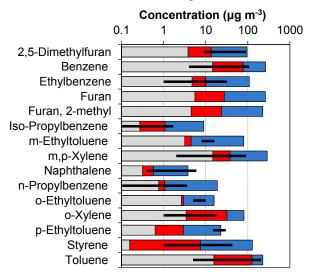


## Exposure to THS via inhalation

#### **Amines and nitriles**

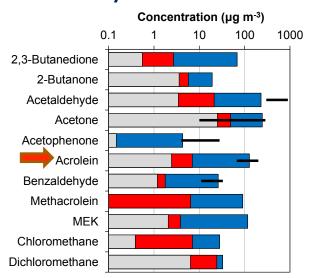


#### **Aromatic hydrocarbons**

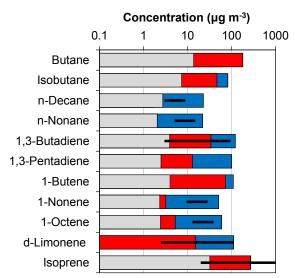




#### **Carbonyls and chlorinated VOCs**



#### **Alkanes and alkenes**



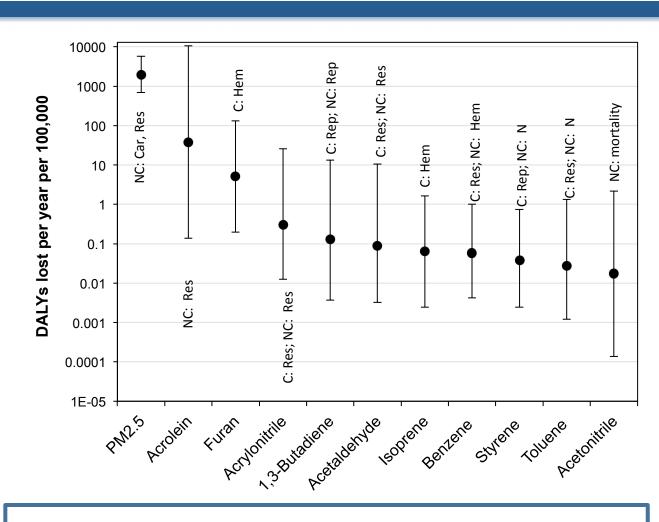
□ acrolein & acrylonitrile exceeded CA reference levels after 18 h (□)

Sleiman et al, ES&T 2014

## Quantifying the harm caused by inhalable THS constituents

#### **DALYs: Disability-Adjusted Life Years**

- Metric developed by WHO to assess the burden of diseases
- Accounts for years of life lost + equivalent years lost to disease or disability
- Integrates different health outcomes
- **Enables identification** and prioritization of top toxicants



C: cancer

D: developmental

N: neurological

Res: respiratory

NC: noncancer

Hem: hematological

Ren: renal

S: skin

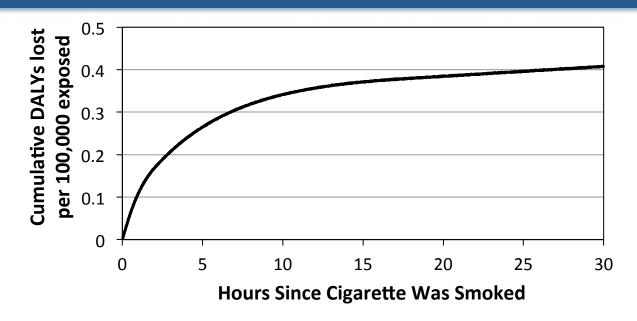
Car: cardiovascular

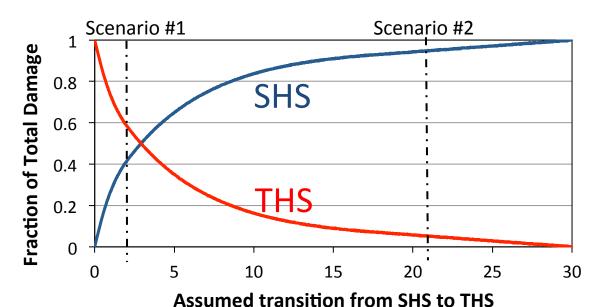
Hep: hepatic

Rep: reproductive

## Apportioning SHS and THS contributions to harm

Between 5% and 60% of the health impacts can be attributed to THS exposure





Sleiman et al, ES&T 2014

## A very high profile thirdhand smoke case...

**POLITICS** 

#### Speaker Paul Ryan Moves Fast to 'Detoxify' Boehner's Smoky Suite

By JENNIFER STEINHAUER NOV. 2, 2015



The speaker's office at the Capitol had been relabeled by Friday, if not redecorated. Stephen Crowley/The New York Times



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WASHINGTON — There are many things Americans cannot yet know about Speaker <u>Paul D. Ryan</u>'s plans for his fancy new digs on Capitol Hill. Dark curtains or sheers? Memorabilia from the 2012 presidential campaign or his first House race in 1998? Will he hang a poster of his favorite band, Rage Against the Machine?

One thing is known: He wants to get rid of the smoke left behind by his predecessor, <u>John A. Boehner</u>. "You know when you ever go to a hotel room or get a rental car that has been smoked in? That's what this smells like," Mr. Ryan said in <u>an interview on NBC's "Meet the Press" on Sunday</u> in reference to the greater with a wide in a formula of particular that the greater interview on NBC's "Meet the Press" on Sunday in reference

## The New York Times

Mr. Ryan said he would most likely rely on an "ozone machine" to "detoxify the environment" of the speaker's office...

## Summary and future steps

☐ THS ages to form irritants, particles and carcinogens. ☐ There are still major information gaps. ☐ Information on composition is limited by sampling and analytical methods; especially for exposure to TSNAs & other toxicants ☐ Health impact assessment should be refined and expanded. ☐ Identify key compounds for further toxicological evaluation ☐ Remediation of THS: does it really work? ☐ Ozonation: short-term and long-term residuals ☐ Develop **guidelines** to help practitioners and the public

## Acknowledgement

- ☐ Anwer Mujeeb & colleagues (TRDRP)
- Brett Singer, Marion Russell,
  Randy Maddalena
  (LBNL-Indoor Environment Group)
- ☐ Musahid Ahmed, Kevin Wilson (LBNL-Advanced Light Source)
- ☐ James F. Pankow (Portland State University)
- ☐ Peyton Jacob III, Suzaynn Schick (UCSF)
- ☐ California THS Consortium partners









# Potentially harmful emissions from electronic cigarettes

H. Destaillats, M. Sleiman, J. M. Logue, N. Montesinos, M. Russell, L. Gundel

Indoor Environment Group
Energy Analysis & Environmental Impacts Division
Energy Technologies Area





## Are e-cigarettes really as innocuous as advertised?

# COMMONLY HEARD CLAIMS:

E-liquids are *healthy* ("food grade", "natural",
 "organic", "kosher", etc)

2. Emissions are just "harmless water vapor"...

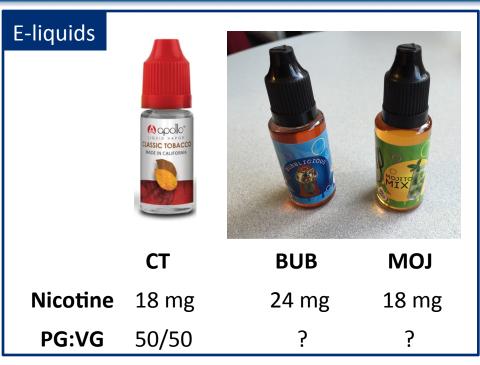






## E-liquids and devices used in this study







## Secondhand vaping

Exhaled mainstream smoke

+

Sidestream smoke (smoldering)



ONLY Exhaled mainstream vapor

Also, topography of vaping can be very different from that of smoking...



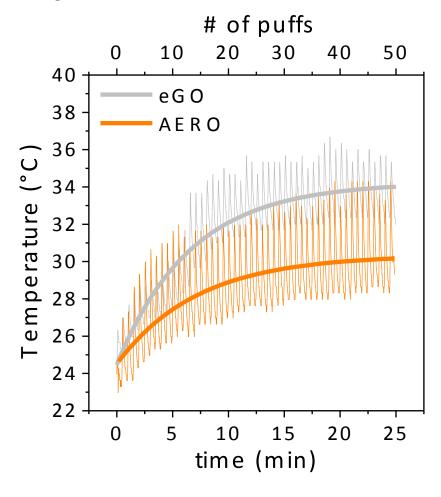
## Vaping in the laboratory

#### <u>Typical e-cigarette topography</u>:

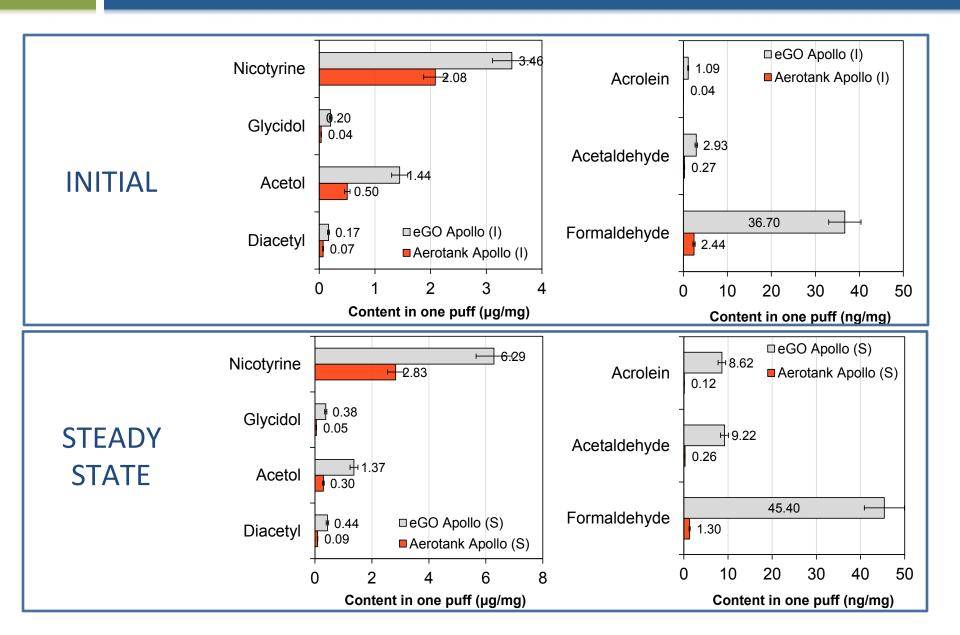
- vaping rate: 2 4 puff min<sup>-1</sup>
- puff volume: ~50 mL
- puff duration: 2 8 s
- inter-puff interval: 18 30 s
- puffing flow rate: ~ 20 mL s<sup>-1</sup>
- Used mechanical system to simulate puffing topography
- Thermocouple placed in mouthpiece
- AERO (2 coils) had consistently lower temperatures than EGO (one coil)
- Samples were collected for two different vaping regimes: INITIAL: first 5 puffs

STEADY-STATE: after puff #30

## Profiles of vapor temperature at 3.8 V



### VOCs emitted at 3.8 V



## Acknowledgement

- ☐ Anwer Mujeeb & colleagues (TRDRP)
- ☐ Brett Singer, Marion Russell,
  Randy Maddalena
  (LBNL-Indoor Environment Group)
- ☐ California THS Consortium partners







#### 2015 (Nov) Berkeley Lab Community Advisory Group Meeting

## Health Impact of Thirdhand Smoke: DNA Damage and Other Adverse Changes

Bo Hang, Ph.D.
Biological Systems & Engineering Division
Lawrence Berkeley National Lab





# Journal of the National Cancer Institute

July 21, 2010, Volume 102, Number 14 inci.oxfordjournals.org

Screening for Breast and Prostate Cancers: Moving Toward Transparency, D.H. Nawman Cigarette Smeking and Colorectal Cancer Risk by Molecularly Defined Subtypes, D. Limsui, R.A. Vierlant, et al. Editorial: Clearing the Air on Smoking and Colorectal Cancer, C.R. Boland, A. Gool Interventions to Promote Repeat Breast Cancer Screening With Mammography: A Syst Review and Meta-Analysis, S.W. Vernon, A. McCusen, et al. Editorial: The Elusive Goal of Maintaining Population Cancer Screening: It is Time for 998 a New Paradigm, J. Mandablatt, D. Buist Effect of Previous Benign Breast Biopsy on the Interpretive Performance of Subsequent Screening Mammography, S.H. Taplin, L. Abraham, et al. Essential Role of TRPC6 Channels in G2/M Phase Transition and Development of 1052

sman Glioma, X. Ding, Z. Ho, et al.

## 2010: my first grant on THS

#### **Health Implications**

Exactly how toxic thirdhand smoke and its derivatives might be is now under investigation. The University of California Tobacco-Related Disease Research Program, which is funded by a state cigarette tax and which supported the work by Gundel and her collabo-

"We also found out that we could not actually measure a limit to the uptake of nicotine in . . . painted wallhoard."

rators, awarded three new grants in June. One recipient, Bo Hang, M.D., Ph.D., a staff scientist at the Lawrence Berkeley National Laboratory, will test the thirdhand smoke's effect on DNA. "If it can cause

DNA damage, then you have the possibility to form cancer," Hang said. "We need to look for the evidence experimentally to assess the genotoxicity of thirdhand smoke. At this stage, that is all we can do."

#### Thirdhand Smoke: Studies Multiply, Catchy Name Raises Awareness

By Rabiya S. Tuma

ealth agencies have warned of the dividuals who thought thirdhand smoke decades. Now a small but growing number of scientists are testing the possible health effects associated with the residue that cigarette smoke deposits on furniture, clothing, and other surfaces, a substance of the news stories, though, focused not on some are calling "thirdhand smoke."

danger of secondhand smoke for was dangerous were more likely to ban smoking entirely from their homes than were individuals who did not perceive a health risk from smoke residue. The study smell to something that could be harmful." attracted widespread media attention. Many the survey results but on the phrase "third-

perception of secondhand smoke was visible tobacco smoke. That is why this concept of thirdhand smoke is so important: It takes something from an annoyance and bad

Not everyone agrees with his definition, though. "As far as I'm aware, almost everyone includes the smoke that has curled off

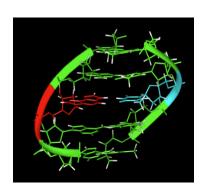


# Is thirdhand smoke (THS) harmful to human health?

THS has become an increasing public health concern. However, little is known about its health impact

Next generation of toxicology tests

Genotoxicity and other biological effects







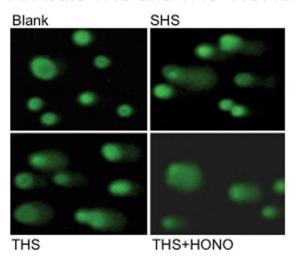
# What have we done regarding the effects of THS exposure?

## 2010-2015

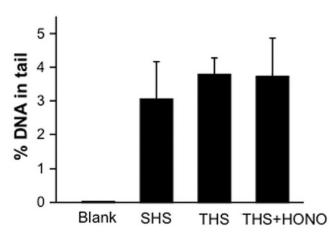
- Genotoxicity studies:
  - DNA strand breaks
  - Oxidative DNA damage (gene damage)
  - > DNA adducts (esp. bulky adducts)
- Metabolomics studies
- Development studies (windows of susceptibility)
- Immunological function studies

### Strand beaks: THS causes DNA strand breaks in human cells

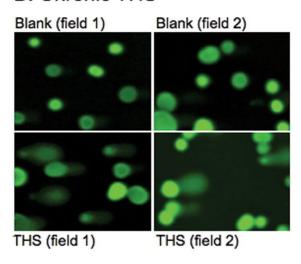
#### A. Acute THS and THS+HONO

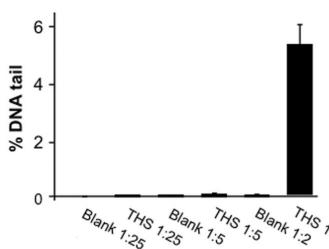


## The Comet assay



#### B. Chronic THS







Bo Hang<sup>1,\*</sup>, Altaf H. Sarker<sup>1</sup>, Christopher Havel<sup>2</sup>, Saikat Saha<sup>3</sup>, Tapas K. Hazra<sup>3</sup>,
Suzavnn Schick<sup>2</sup>, Pevton Jacob III<sup>2</sup>, Virender K. Rehan<sup>4</sup>, Ahmed Chenna<sup>5</sup>, Divva Sharan<sup>1</sup>.

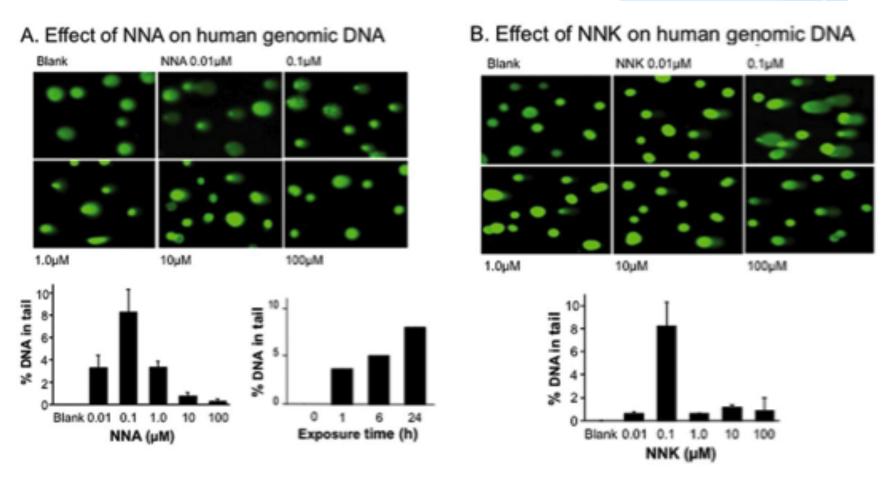
니 'To whom correspondence should be addressed. Department of Cancer & DNA Damage Responses, Life Sciences Division, Lawrence Berkeley National Laboratory, 1 Cyclotron Rd, Berkeley, CA 94720, USA. Tel: +1 510-495-2537; Fax: +1 510-486-6488; Email:

Mohamad Sleiman<sup>6</sup>, Hugo Destaillats<sup>6</sup> and Lara A. Gundel<sup>6</sup>

+ Author Affiliations

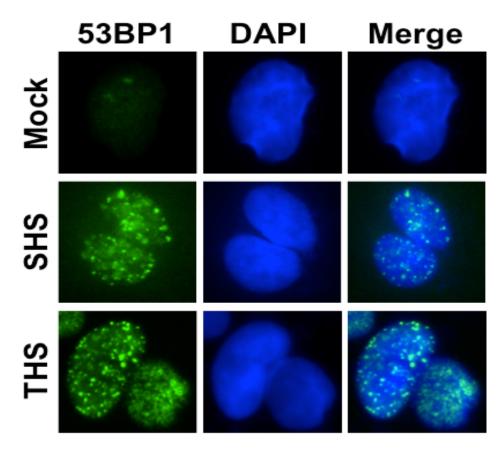
mutagenesis

#### NNA induces DNA strand breaks in human cells



These effective dose ranges observed as per milliliter are comparable with the total amounts of NNA and NNK deposited per square meter of the real life surface area

# Strand beaks: DNA double-strand breaks induced by exposure to THS

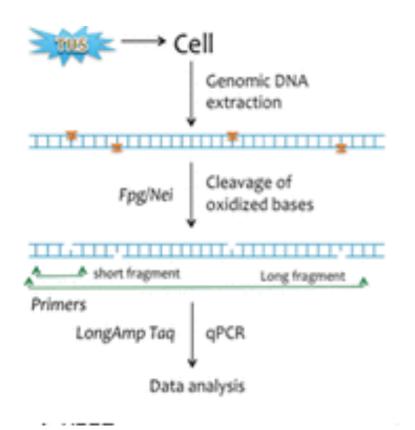


53BP1/γ-H2AX foci formation



DSBs are most genotoxic DNA lesions leading to genome instability, which could causes cancer

# Gene damage: THS induces oxidative DNA damage In genes of cultured human cells



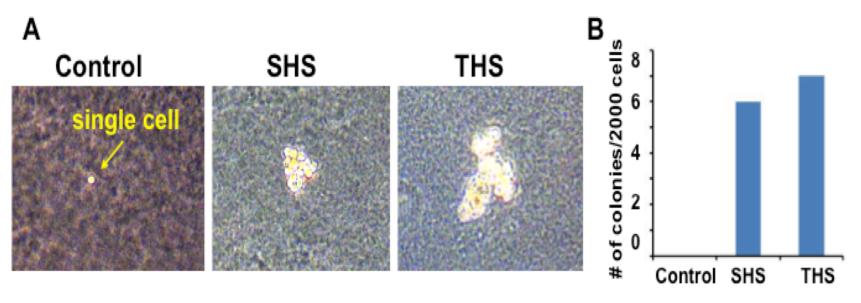
THS exposure causes oxidative DNA damage in both in vitro and in vivo systems

Oxidative DNA damage can lead to disease-causing mutations, such as in cancer

Long amplicon – qPCR assay

# Cell transformation: THS induces anchorage-independent growth in 3D culture

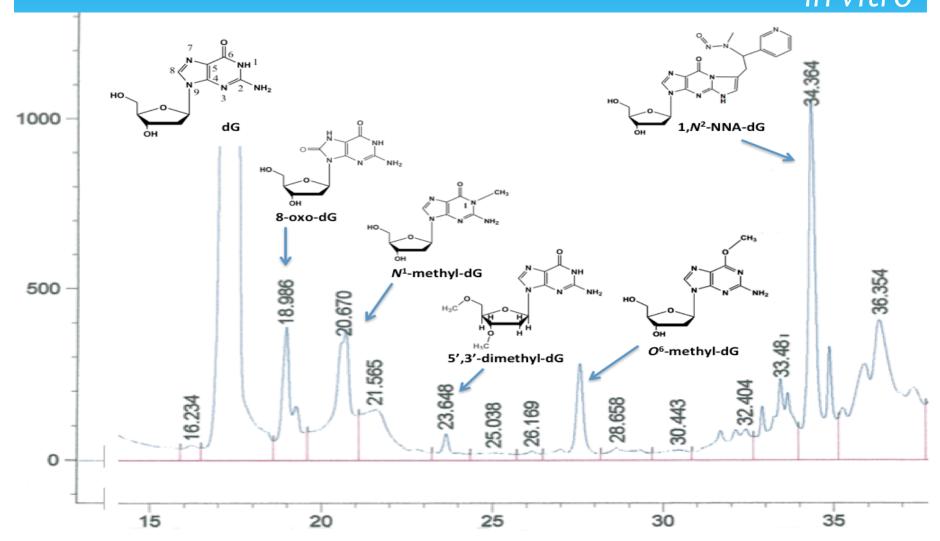
## Soft agar assay



Colony formation

The soft agar assay was used to confirm cellular anchorageindependent growth in vitro, which is the tumorigenic potential of transformed cells.

# DNA adducts: Identification of NNA-dG adducts formed in vitro



THS compound NNA forms a novel covalent dG adduct, 1,N2-NNA-dG

#### RESEARCH

#### RESEARC

# MAJOR 'THIRD-HAND SMOKE' COMPOUND CAUSES DNA DAMAGE—AND POTENTIALLY CANCER

eftover cigarette smoke that clings to walls and furniture is a smelly nuisance, but now research suggests that it could pose a far more serious threat, especially to young children who put toys and other smoke-affected items into their mouths. Scientists reported today that one compound from this "third-hand smoke," which forms when second-hand smoke reacts with indoor air, damages DNA and sticks to it in a way that could potentially cause cancer.

Bo Hang, who presented the research, said that although the idea of third-hand smoke made its debut in research circles just a few years ago in

2009, evidence already strongly suggests it could threaten human health.

"The best argument for instituting a ban on smoking indoors is actually third-hand smoke," said Hang, a scientist at Lawrence Berkeley National Laboratory (LBNL).

Researchers have found that many of the more than 4,000 compounds in second-hand smoke, which wafts through the air as a cigarette is smoked, can linger indoors long after a cigarette is stubbed out. Based on studies led by Hugo Destaillats, also at LBNL, these substances can go on to react with indoor pollutants such as ozone and nitrous acid, creating brand-new compounds, some of which may be carcinogenic.

One of those compounds goes by the acronym NNA. Hang's research has shown that NNA, a tobacco-specific nitrosamine, locks onto DNA to form a



smoke that is inhaled as a person breathes in directly from the cigarette, making the connection between third-hand smoke or NNA and cancer could take a long time, Hang said.

But early research into its nature, exposure and health effects is compelling enough that a research consortium dedicated to investigating third-hand smoke was formed in California in 2010. That consortium helped fund Hang's work on NNA-induced DNA damage, which he said could eventually be used as biomarkers to identify people who have been exposed to thirdhand smoke.

The biggest potential health risk is for babies and toddlers, he noted. As they crawl and put their hands or toys in their mouths, they could touch, swallow or inhale compounds from third-hand smoke. Their small size and early developmental stage make them more vulnerable than adults to the effects of environmental hazards.

Although many public places prohibit smoking, Hang noted that people can still smoke in most rental apartments and private residences — and smoking remains a huge public health issue. In 2011, nearly 44 million American adults reported smoking cigarettes, which ranks as the leading cause of preventable death in this country. And 34 million people smoke every day, according to data from the Centers for Disease Control & Prevention.

# THS is becoming



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#### Pioneering study claims THIRD-HAND

# Thirdhand Smoke Spurs DNA Damage, Study Finds

Posted: 06/24/2013 7:34 am EDT | Updated: 06/24/2013 10:41 pm EDT

We know firsthand smoke is had now, research THE over

hand smoke is also bad. But ne surface-clinging residue left to our DNA.

is mutagenic," study eley National laboratory, said

in a st thirdh surfaces, some of the chemical compounds in thirdh surfaces, and when those surfaces are clothing or carpets, the danger to children is especially serious."

The study, published in the journal Mutagenesis, doesn't just show that thirdhand smoke can harm cells -- it also shows that the harm it can cause could become worse with time.

### 

a national

concern

#### 'Thirdhand' smoke poses cancer risk

By John Roberts / Published March 17, 2014 / FoxNews.com



# THE TIMES OF INDIA

igering smoke can harm DNA

eya Sinha, TNN Jun 22, 2013, 05.13AM IST

eya Sinna,

: Touch | Smoking | Genetic | (

IDON: The direct hazards of known and so are the ill-effects hand smoke. But scientists have first time that third-hand smoke that clings to hair, skin, clothes walls, furniture, drapes, beddin long after smoking has stopped genetic damage to human cells an independent causative ager New research out of the Lawrence Berkeley National Laboratory has found that the residue from smoking indoors – so-called "thirdhand smoke" – has the potential to cause cancer.

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Science ... AND NBC NEWS.com

Thirdhand Smoke Damages
Human Cells

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DNA damage seen from "thirdhand smoke"

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**Systemwide News** 

June 2013

#### Legislators tap grad students for expertise



After presentations at Graduate Research Day in Sacramento, legislators ask students for input on issues ranging from urban planning to protecting marine ecosystems.

Our University

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For 20 years, UC's California Breast Cancer Research Program has fought the disease through innovative research and community outreach.

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- UC Irvine ranked fifth in world among universities und 50 years old
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#### **National Public Radio:**

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#### **National Geographic:**

Thirdhand smoke is real - and risky to your health (2014.3.20)

**Men's Health:** Health danger: thirdhand smoke (2014.3.24)

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# Thirdhand Smoke Is Real—And Risky to Your Health

Indoor cigarette smoke combines with air pollutants to form compounds that might cause cancer—and that can linger for decades.













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# California Bill Targets Third-Hand Smoke In Home Day Care Centers

April 21, 2014 4:21 PM



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- Our findings show that thirdhand smoke present health hazards and potential cancer risk to the public
- Our findings have raised awareness around the health issues of thirdhand smoke and have already led to a change in state policy

### 2015 (Nov) Berkeley Lab Community Advisory Group Meeting

# Health Impact of Thirdhand Smoke: DNA Damage and Other Adverse Changes

Bo Hang, Ph.D.
Biological Systems & Engineering Division
Lawrence Berkeley National Lab





# Journal of the National Cancer Institute

July 21, 2010, Volume 102, Number 14 inci.oxfordjournals.org

Screening for Breast and Prostate Cancers: Moving Toward Transparency, D.H. Nawman Cigarette Smeking and Colorectal Cancer Risk by Molecularly Defined Subtypes, D. Limsui, R.A. Vierlant, et al. Editorial: Clearing the Air on Smoking and Colorectal Cancer, C.R. Boland, A. Gool Interventions to Promote Repeat Breast Cancer Screening With Mammography: A Syst Review and Meta-Analysis, S.W. Vernon, A. McCusen, et al. Editorial: The Elusive Goal of Maintaining Population Cancer Screening: It is Time for 998 a New Paradigm, J. Mandablatt, D. Buist Effect of Previous Benign Breast Biopsy on the Interpretive Performance of Subsequent Screening Mammography, S.H. Taplin, L. Abraham, et al. Essential Role of TRPC6 Channels in G2/M Phase Transition and Development of 1052

sman Glioma, X. Ding, Z. Ho, et al.

# 2010: my first grant on THS

#### **Health Implications**

Exactly how toxic thirdhand smoke and its derivatives might be is now under investigation. The University of California Tobacco-Related Disease Research Program, which is funded by a state cigarette tax and which supported the work by Gundel and her collabo-

"We also found out that we could not actually measure a limit to the uptake of nicotine in . . . painted wallhoard."

rators, awarded three new grants in June. One recipient, Bo Hang, M.D., Ph.D., a staff scientist at the Lawrence Berkeley National Laboratory, will test the thirdhand smoke's effect on DNA. "If it can cause

DNA damage, then you have the possibility to form cancer," Hang said. "We need to look for the evidence experimentally to assess the genotoxicity of thirdhand smoke. At this stage, that is all we can do."

#### Thirdhand Smoke: Studies Multiply, Catchy Name Raises Awareness

By Rabiya S. Tuma

ealth agencies have warned of the dividuals who thought thirdhand smoke decades. Now a small but growing number of scientists are testing the possible health effects associated with the residue that cigarette smoke deposits on furniture, clothing, and other surfaces, a substance of the news stories, though, focused not on some are calling "thirdhand smoke."

danger of secondhand smoke for was dangerous were more likely to ban smoking entirely from their homes than were individuals who did not perceive a health risk from smoke residue. The study smell to something that could be harmful." attracted widespread media attention. Many the survey results but on the phrase "third-

perception of secondhand smoke was visible tobacco smoke. That is why this concept of thirdhand smoke is so important: It takes something from an annoyance and bad

Not everyone agrees with his definition, though. "As far as I'm aware, almost everyone includes the smoke that has curled off

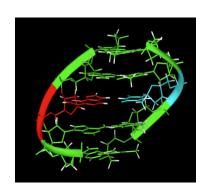


# Is thirdhand smoke (THS) harmful to human health?

THS has become an increasing public health concern. However, little is known about its health impact

Next generation of toxicology tests

# Genotoxicity and other biological effects







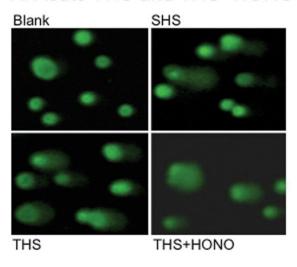
# What have we done regarding the effects of THS exposure?

# 2010-2015

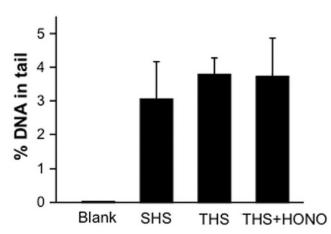
- Genotoxicity studies:
  - DNA strand breaks
  - Oxidative DNA damage (gene damage)
  - > DNA adducts (esp. bulky adducts)
- Metabolomics studies
- Development studies (windows of susceptibility)
- Immunological function studies

## Strand beaks: THS causes DNA strand breaks in human cells

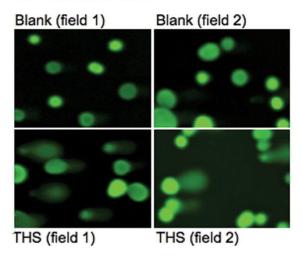
#### A. Acute THS and THS+HONO

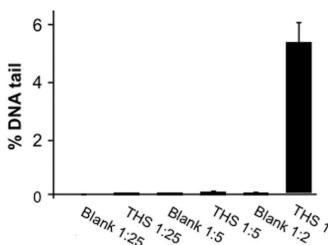


## The Comet assay



#### B. Chronic THS







Bo Hang<sup>1,\*</sup>, Altaf H. Sarker<sup>1</sup>, Christopher Havel<sup>2</sup>, Saikat Saha<sup>3</sup>, Tapas K. Hazra<sup>3</sup>,
Suzavnn Schick<sup>2</sup>, Pevton Jacob III<sup>2</sup>, Virender K. Rehan<sup>4</sup>, Ahmed Chenna<sup>5</sup>, Divva Sharan<sup>1</sup>.

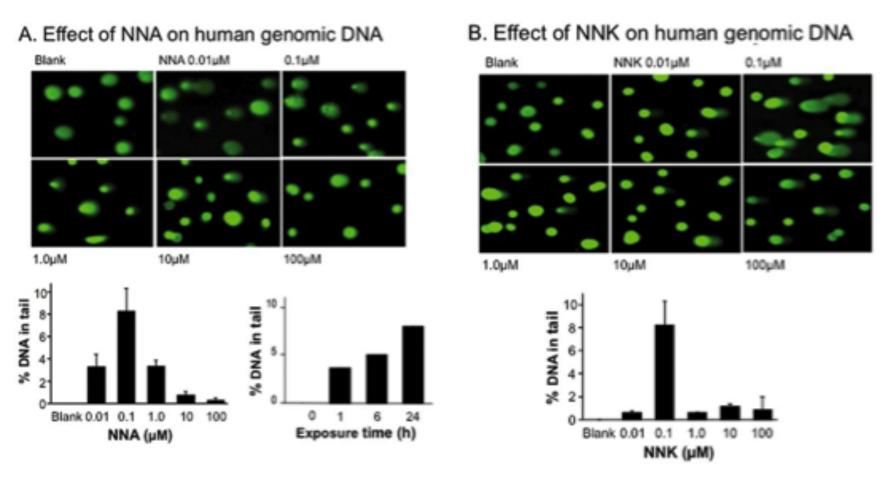
니 'To whom correspondence should be addressed. Department of Cancer & DNA Damage Responses, Life Sciences Division, Lawrence Berkeley National Laboratory, 1 Cyclotron Rd, Berkeley, CA 94720, USA. Tel: +1 510-495-2537; Fax: +1 510-486-6488; Email:

Mohamad Sleiman<sup>6</sup>, Hugo Destaillats<sup>6</sup> and Lara A. Gundel<sup>6</sup>

+ Author Affiliations

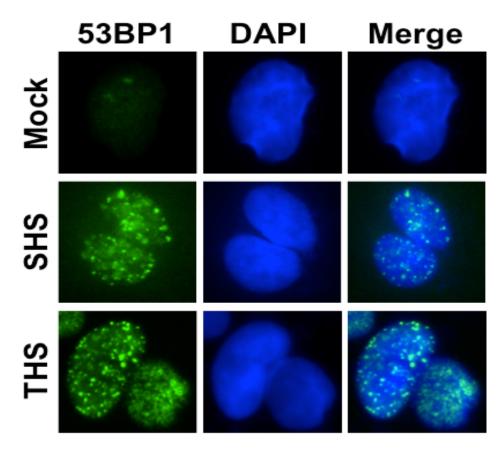
mutagenesis

### NNA induces DNA strand breaks in human cells



These effective dose ranges observed as per milliliter are comparable with the total amounts of NNA and NNK deposited per square meter of the real life surface area

# Strand beaks: DNA double-strand breaks induced by exposure to THS

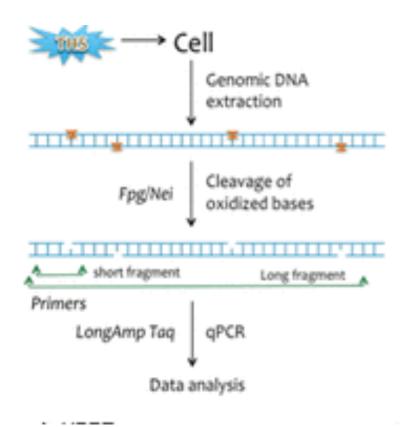


53BP1/γ-H2AX foci formation



DSBs are most genotoxic DNA lesions leading to genome instability, which could causes cancer

# Gene damage: THS induces oxidative DNA damage In genes of cultured human cells



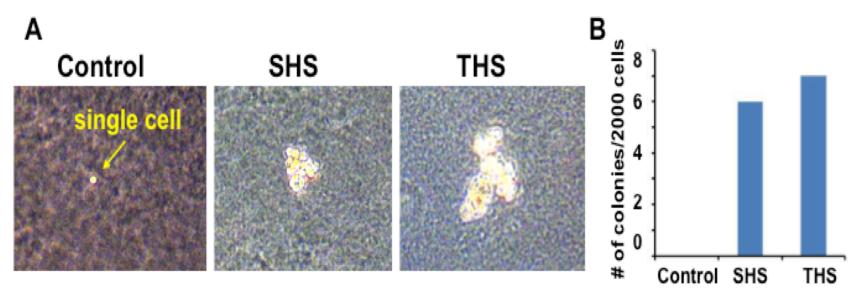
THS exposure causes oxidative DNA damage in both in vitro and in vivo systems

Oxidative DNA damage can lead to disease-causing mutations, such as in cancer

Long amplicon – qPCR assay

# Cell transformation: THS induces anchorage-independent growth in 3D culture

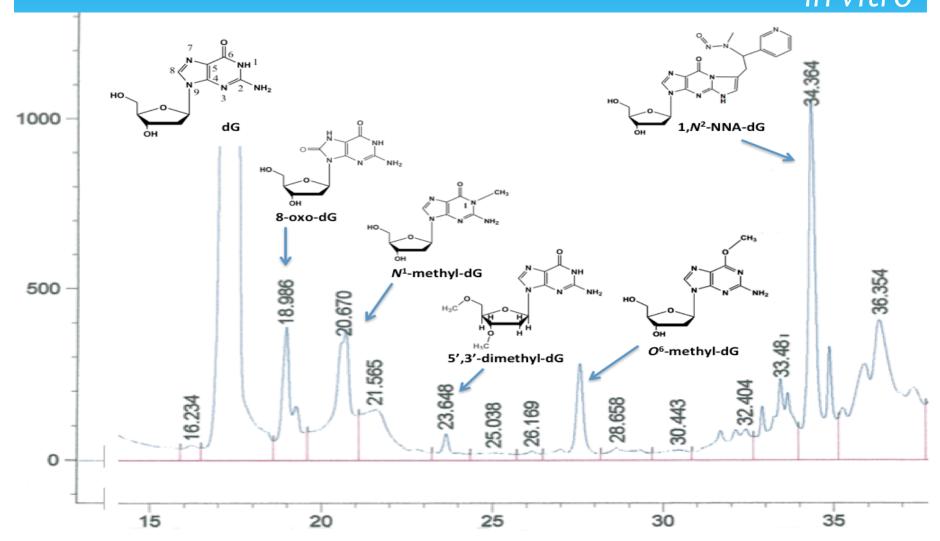
# Soft agar assay



Colony formation

The soft agar assay was used to confirm cellular anchorageindependent growth in vitro, which is the tumorigenic potential of transformed cells.

# DNA adducts: Identification of NNA-dG adducts formed in vitro



THS compound NNA forms a novel covalent dG adduct, 1,N2-NNA-dG

#### RESEARCH

#### RESEARC

# MAJOR 'THIRD-HAND SMOKE' COMPOUND CAUSES DNA DAMAGE—AND POTENTIALLY CANCER

eftover cigarette smoke that clings to walls and furniture is a smelly nuisance, but now research suggests that it could pose a far more serious threat, especially to young children who put toys and other smoke-affected items into their mouths. Scientists reported today that one compound from this "third-hand smoke," which forms when second-hand smoke reacts with indoor air, damages DNA and sticks to it in a way that could potentially cause cancer.

Bo Hang, who presented the research, said that although the idea of third-hand smoke made its debut in research circles just a few years ago in

2009, evidence already strongly suggests it could threaten human health.

"The best argument for instituting a ban on smoking indoors is actually third-hand smoke," said Hang, a scientist at Lawrence Berkeley National Laboratory (LBNL).

Researchers have found that many of the more than 4,000 compounds in second-hand smoke, which wafts through the air as a cigarette is smoked, can linger indoors long after a cigarette is stubbed out. Based on studies led by Hugo Destaillats, also at LBNL, these substances can go on to react with indoor pollutants such as ozone and nitrous acid, creating brand-new compounds, some of which may be carcinogenic.

One of those compounds goes by the acronym NNA. Hang's research has shown that NNA, a tobacco-specific nitrosamine, locks onto DNA to form a



smoke that is inhaled as a person breathes in directly from the cigarette, making the connection between third-hand smoke or NNA and cancer could take a long time, Hang said.

But early research into its nature, exposure and health effects is compelling enough that a research consortium dedicated to investigating third-hand smoke was formed in California in 2010. That consortium helped fund Hang's work on NNA-induced DNA damage, which he said could eventually be used as biomarkers to identify people who have been exposed to thirdhand smoke.

The biggest potential health risk is for babies and toddlers, he noted. As they crawl and put their hands or toys in their mouths, they could touch, swallow or inhale compounds from third-hand smoke. Their small size and early developmental stage make them more vulnerable than adults to the effects of environmental hazards.

Although many public places prohibit smoking, Hang noted that people can still smoke in most rental apartments and private residences — and smoking remains a huge public health issue. In 2011, nearly 44 million American adults reported smoking cigarettes, which ranks as the leading cause of preventable death in this country. And 34 million people smoke every day, according to data from the Centers for Disease Control & Prevention.

# THS is becoming

2014



a national concern

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Pioneering study claims THIRD-HAND

#### **Thirdhand Smoke Spurs DNA** Damage, Study Finds

Posted: 06/24/2013 7:34 am EDT | Updated: 06/24/2013 10:41 pm EDT

We know firsthand smoke is had

hand smoke is also bad. But ne surface-clinging residue left

is mutagenic," study eley National laboratory, said

mes, some of the chemical compounds in in a st thirdh among the most potent carcinogens there are. They stay on surfaces, and when those surfaces are clothing or carpets, the danger to children is especially serious."

The study, published in the journal Mutagenesis, doesn't just show that thirdhand smoke can harm cells -- it also shows that the harm it can cause could become worse with time.

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美国华人科学家主导研究发现三手烟损害人体基因

[提要] (记者 刘丹)一项由美国华人科学家主导的跨学科研究发现,三手烟在人体细胞会引起基 因突变,从而造成癌症和其他疾病的可能性。杭渤26日接受中新社记者访问时说。三手烟指吸烟

#### 'Thirdhand' smoke poses cancer risk

By John Roberts / Published March 17, 2014 / FoxNews.com



# THE TIMES OF INDIA

# igering smoke can harm DNA

eya Sinha, TNN Jun 22, 2013, 05.13AM IST

: Touch | Smoking | Genetic | (

New research out of the Lawrence Berkeley National Laboratory has found that the residue from smoking indoors - so-called "thirdhand smoke" - has the potential to cause cancer.

NDON: The direct hazards of known and so are the ill-effects hand smoke. But scientists have

first time that third-hand smok that clings to hair, skin, clothes walls, furniture, drapes, beddin long after smoking has stopped genetic damage to human cells an independent causative ager



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CBSNews.com / CBS Evening News / CBS This Morning / 48 Hours / 60 Minutes / Sunday Morning / Face The Nation

Systemwide News

#### Legislators tap grad students for expertise



June 2013

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After presentations at Graduate Research Day in Sacramento, legislators ask students for input on issues ranging from urban planning to protecting marine

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#### Fighting breast cancer



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**DNA** damage seen from "thirdhand smoke"

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April 21, 2014 4:21 PM



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## Extended Stay

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